Rita and the four Gs

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In Praise of Imperfection: My Life and Work. By Rita Levi-Montalcini. Translated by Luigi Attardi. *Sloan Foundation Science Series/Basic Books:1988. Pp.220. $18.95.*

RITA Levi-Montalcini received the Nobel Prize for Physiology or Medicine in 1986, together with Stanley Cohen, for their discovery of growth factors, made 30 years earlier while working together at Washington University in St Louis. This book recalls Levi-Montalcini's life from her childhood in Turin to her return to Italy from the United States in 1963. Its title derives from a poem by Yeats:

The intellect of man is forced to choose
Perfection of the life, or of the work,
And if it take the second must refuse
A heavenly mansion, raging in the dark.

Levi-Montalcini chose the work.

André Lwoff wrote that: "The scientist's art is first of all to find himself a good master", to which I should add "and next, to find himself a good problem". Levi-Montalcini found her problem in a laboratory rigged up in her bedroom during the Second World War, when Mussolini's antisemitic legislation, a cowardly copy of the German, forced Turin University to expel all Jews, including her professor of anatomy Giuseppe Levi. He was the master who had aroused her interest in the nervous system when she was an intern, worked with her in her improvised laboratory, and encouraged her for the rest of his long life. They set out to analyse how excision of as yet non-innervated limbs from early chick embryos affected development of motor cells in the spinal cord and of sensory cells in the dorsal root ganglia, and were led to suspect that the limbs release a tropic factor that is conveyed by the growing axons to their cell bodies. After the war their publication came to the attention of Viktor Hamburger, a German émigré and pupil of the great embryologist Hans Spemann. Hamburger invited Levi-Montalcini to spend a semester with him at St Louis. That semester was to become 16 years.

The decisive observations came in an experiment that illustrates the importance of the prepared mind. Elmer Bueker, a former pupil of Hamburger, sent him an article which described how a mouse sarcoma, grafted on to a chick embryo, had become innervated by fibres from the embryo. Bueker concluded that the tumour had provided more ample terrain for the growth of the nerve fibres than the nearby embryonic limb, but Levi-Montalcini thought otherwise. In a euphoric mood, she dropped all current research in order to repeat Bueker's work. On being grafted to her embryos, the tumours Bueker had used became innervated as Bueker had described, but another tumour sent to her (by mistake?) produced a far more dramatic effect. It caused the non-innervated organs of the embryo, including its viscera and blood vessels, to be invaded by large bundles of nerve fibres. She writes:

Wide-eyed awareness — Rita Levi-Montalcini in 1920.

This observation indicated that the tumour had released a humoral, a fluid, factor able both to accelerate differentiative processes in sympathetic and, to a lesser degree, sensory cells; and to cause excessive production, as well as the quantitatively and qualitatively abnormal distribution of nerve fibres.

What was that factor?

Its nature revealed itself by a remarkable stroke of luck, after Stanley Cohen, then a young biochemist, had joined her at St Louis. In experiments carried out in Carlos Chagas and Hertha Meyer's laboratory at Rio de Janeiro, the author had established that extracts of mouse tumours induced the formation of haloes of nerve fibrils around cultured sensory ganglia, but only if the tumours had first been transplanted into and then excised from chick embryos. Levi-Montalcini and Cohen spent a year trying to extract enough of the factor from such transplanted mouse sarcomas to characterize it, and thought it was a nucleoprotein. When Cohen wondered if the nucleic acid might be a contaminant, Arthur Kornberg, then at St Louis, suggested treating the extract with snake venom whose phosphodiesterase breaks down nucleic acid; instead of destroying the activity the snake venom raised it spectacularly. It turned out that it contained a several thousand times greater concentration of the growth factor than the mouse tumours. This discovery allowed Cohen to isolate and characterize the factor and provided Levi-Montalcini with pure factor to inject into her embryos. Had they been able to buy pure phosphodiesterase from Sigma, they would never have discovered this.

The first part of the book is an interesting documentary of life in a Jewish middle-class family in fascist Italy before and during the Second World War, especially during the Nazi terror, when the Levis were hidden in Florence under false names by good-natured, courageous gentiles who pretended not to know that they were Jews. A far greater proportion of Jews survived in Italy than in any other country of continental Europe, because gentiles helped and hid them, often at the risk of their lives.

Paul Ehrlich has said that success in research needs four Gs: Glück, Geduld, Geschick und Geld (luck, patience, skill and money). Levi-Montalcini's book shows that she had the first three in good measure and that she needed little of the fourth. □

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